DETAILED ACTION

Application Status

Claims 7-30 and 32-39 of the instant application are pending. Claims 7-28 and 30 are withdrawn pursuant to Applicant's Amendment, filed 04/17/2009. Accordingly, instant claims 29 and 32-39, drawn to a method of treatment for improving the absorption of amino acids in a vertebrate, comprising administering α-ketoglutarate, are presented for examination on their merits.

Upon reconsideration, the Non-Responsive Communication, mailed 07/09/2009, is ***vacated***.

Applicant's Arguments, filed 04/17/2009, have been fully considered. Rejections/objections not reiterated from previous Office Actions are hereby ***withdrawn***. The following rejections/objections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Applicant's Amendment

Applicant's Amendment, filed 04/17/2009, wherein the specification and claims 29, 30, 32, 34-36 and 39 are amended, 7-28 and 30 are withdrawn, and claims 1-6 and 31 are canceled, is acknowledged.

Specification

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract of the disclosure is objected to use of legal phraseology, “comprising” (line 1).

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Correction is required.

Response to Arguments

The rejection of claims 29, 30, 31 (in part) and 32-39, previously rejected under 35 U.S.C. 112, first paragraph, is hereby ***withdrawn*** pursuant to Applicant's Amendment, filed 04/17/2009.

The rejection of claims 32-39, previously rejected under 35 U.S.C. 112, first paragraph, is hereby ***withdrawn*** pursuant to Applicant's Amendment, filed 04/17/2009.

The rejection of claims 31, 35 and 39, previously rejected under 35 U.S.C. 112, second paragraph, is hereby ***withdrawn*** pursuant to Applicant's Amendment, filed 04/17/2009.

Claim Rejections - 35 USC § 112

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim 38 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim language of withdrawn instant claim 30 is directed to wherein the metal salt of AKG is selected from CaAKG, $CA(AKG)_2$, and NaAKG. However, claim 38, drawn to wherein the amino acid is an essential amino acid, is dependent from claim 30.

Clarification is required.

Claim Rejections - 35 USC § 102

Claims 29, 32 and 37-39 were rejected under 35 U.S.C. 102(b) as being anticipated by Riedel *et al*. (Nephron, Vol. 74, No. 2, pages 261-265; 1996; Cited by Applicant).

With regard to instant claims 29, 32 and 37-39, Riedel *et al*. disclose, in the Abstract, wherein the free amino acids and α-ketoacids in plasma were determined by fluorescence HPLC to assess the effect of α-ketoglutarate administration in combination

with the phosphate binder calcium carbonate on the amino acid metabolism. In the instant excerpt, Riedel *et al*. further disclose during one year of therapy in parallel to inorganic phosphate, urea in plasma decreased significantly, and amino acids, e.g., histadine, arginine and proline, increased (instant claims 29, 38 and 39). Furthermore, Riedel *et al*. concluded that the administration of α-ketoglutarate with calcium carbonate effectively improves amino acid metabolism in hemodialysis patients (e.g., human being or mammal; instant claims 32 and 37). In the last paragraph of the Introduction, Riedel *et al*. disclose wherein the aim of the study was to clarify whether or not the reference medication, in phosphate-binding doses in hemodialysis patients, is able to improve amino acid metabolism and malnutrition. In Figures 1 and 2, and column two, last paragraph, on page 263, Riedel *et al*. disclose where amino acids, such as leucine and lysine, showed significantly increased plasma concentrations (instant claims 38 and 39). Additionally, Riedel *et al*. disclose, on page 264, column two, lines 14-20 of text, wherein the significant increase of plasma concentrations of proline, for example, is due to the consequence of increased production of glutamate via transamination of the supplemented α-ketoglutarate.

Accordingly, instant claims 29, 32 and 37-39 are anticipated by Riedel *et al.*, and properly rejected under 35 U.S.C. 102(b).

Applicant's Arguments

Applicant alleges that Riedel *et al*. disclose the use of alpha-ketoglutarate (AKG) together with calcium carbonate to hemodialysis patients improving their amino-acid

metabolism, and the invention according to claim 29 involves use of AKG to improve absorption of amino acids, wherein such absorption occurs from the gut to the bloodstream. Applicant further alleges Riedel *et al*. does not teach, disclose or suggest a method of using AKG to improve the absorption of amino acids.

Examiner's Response

Applicant's Arguments, filed 04/17/2009, have been fully considered but they are not persuasive.

The Examiner acquiesces with Applicant in that Riedel *et al*. disclose the administration of α-ketoglutarate with calcium carbonate effectively improves amino acid metabolism in hemodialysis patients. The open language of the present claims allows for the additional administration of other agents. However, subsequently, from the administration of, at least, the α-ketoglutarate, the plasma concentrations of proline, leucine and lysine were significantly increased. See *supra*. Therefore, one of ordinary skill in the art, at the time of the invention, would have construed wherein the absorption of the essential amino acids, which must be supplied in the diet, are improved.

Accordingly, instant claims 29, 32 and 37-39 are anticipated, and the rejection is maintained.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 29 and 32-39 were rejected under 35 U.S.C. 103(a) as being unpatentable over Riedel *et al*. (Nephron, Vol. 74, No. 2, pages 261-265; 1996; Cited by Applicant), as applied to claims 29, 32 and 37-39 above, and further in view of Plouvier *et al*. (US Patent Application Publication No. 2004/0127413A1) and Shiflett *et al*. (Journal of Nutrition, Vol. 98, pages 420-426; 1969).

With regard to instant claims 29, 32 and 37-39, the teachings of Riedel *et al*. have been set forth *supra*.

With regard to instant claims 33-36, Riedel *et al*. fail to disclose specifically wherein the vertebrate is a rodent, i.e., a rat, a bird, i.e., a chicken, a farm animal, i.e., a cow, or a domestic pet, i.e., a dog. However, Plouvier *et al*. disclose in reference claims 1-3, 5-9, 33, 35 and 42, pages 10 and 11, a method of treating a mammal in need of treatment, comprising administering a therapeutically effective amount of the enteric composition comprising at least one compound of the empirical formula (I) to the mammal, i.e., human being, suffering from malnourishment. In the instant excerpt,

Plouvier *et al*. further disclose wherein the empirical formula (I), i.e., $(X)n_1Y(X)n_2$, comprises wherein X is ornithine, lysine, arginine, proline or glutamine, wherein n_1 is 1 and n_2 is 0, and wherein Y is alpha-ketoglutaric acid (instant claim 29).

Plouvier *et al*. fail to disclose specifically wherein the mammal is a vertebrate mentioned *supra*. However, one of ordinary skill in the art, at the time of the invention would have construed the term "mammal", which is a class of vertebrate animals whose name is derived from their distinctive feature, mammary glands, to encompass a rat, a cow or a dog, for example.

Plouvier *et al*. fail to disclose specifically wherein vertebrate is a bird, e.g., chicken. However, Shiflett *et al*. disclose, in the Abstract, a study to test the effect of vitamin B_6 deficiency on levels of leucine transaminase activity in various tissues of chicks. In the instant excerpt, Shiflett *et al*. further disclose that after 8 days, chicks fed a deficient diet, comprising zero or 1.2 mg pyridoxine·HCl/100 g, showed evidence of severe vitamin B_6 deficiency, which resulted in anorexia and retarded growth, for example. Furthermore, Shiflett *et al*. disclose where leucine transaminase activity was significantly decreased in the kidney of chicks fed the deficient diet for 1.5 days. Additionally, Shiflett *et al*. disclose, on page 420, column 1, line 1-10, wherein the purpose of the study was to investigate the unreported effect of vitamin B_6 deficiency on the activity of the leucine transaminases, which catalyze the transamination of the branched-chain amino acids essential for animals, with alpha-ketoglutaric acid.

Therefore, a skilled artisan, at the time of the invention, would have envisaged the method of treating malnutrition in a vertebrate, comprising administering a

composition comprising α-ketoglutaric acid, as disclosed by Riedel *et al*., in view of Plouvier *et al*. One of ordinary skill in the art would have been motivated to combine the teachings of the aforementioned references when seeking a therapeutically effect medicament, with doses low enough to avoid unwanted side effects, in the treatment of a malnourished vertebrate. A skilled artisan, at the time of the invention, would have also been motivated to use the methods, wherein the vertebrate is a chicken, for example, as disclosed by Shiflett *et al*., when contemplating the treatment of malnutrition, as a result of anorexia, in an animal destined for use in food production, for example. It would have been obvious to one of ordinary skill in the art, at the time of the invention, because the combined teachings of the prior art are fairly suggestive of the claimed invention.

Accordingly, the instant invention, as claimed in claims 29 and 32-39, is *prima facie* obvious over the combination of the aforementioned teachings.

Applicant's Arguments

Applicant alleges Riedel *et al*. does not teach, disclose or suggest a method of using AKG to improve the absorption of amino acids from the gut, and neither Plouvier *et al*. nor Shiflett *et al*. cure the deficit found in Riedel *et al*. Applicant further alleges that a person of skill in the art would find no guidance of the same from the references to solve the problem of claim 29.

Examiner's Response

Applicant's Arguments, filed 04/17/2009, have been fully considered but they are not persuasive.

The Examiner acquiesces with Applicant in that Riedel *et al*. disclose the administration of α-ketoglutarate with calcium carbonate effectively improves amino acid metabolism in hemodialysis patients. The open language of the present claims allows the additional administration of other agents. However, subsequently, from the administration of, at least, the α-ketoglutarate, the plasma concentrations of proline, leucine and lysine were significantly increased. See *supra*. Additionally, Plouvier *et al*. and Shiflett *et al*. were relied upon as teachings of α-ketoglutaric acid administration to a mammal and chicken, respectively, in need of such treatment. Therefore, one of ordinary skill in the art, at the time of the invention, would have construed wherein the absorption of the essential amino acids, which must be supplied in the diet, are improved.

Accordingly, the instant invention, as claimed in claims 29, 32 and 37-39, is *prima facie* obvious over the aforementioned teachings, and the rejection is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NELSON C. BLAKELY III whose telephone number is (571) 270-3290. The examiner can normally be reached on Mon - Thurs, 7:00 am - 5:30 pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Phyllis G. Spivack/
Primary Examiner, Art Unit 1614
August 6, 2009

/N. C. B. III/
Examiner, Art Unit 1614